

Amendments to the Specification

Please replace the paragraph beginning at page 20, line 11, with the following amended paragraph.

--Figure 44. Structure-function relationship for NaCT. Fig. 44A demonstrates the influence of Li^+ (10 mM) on the uptake of citrate (20 μM) via wild type human and rat NaCTs and the chimeric transporter in which the region containing the amino acids 496-516 in human NaCT has been replaced with the corresponding region from rat NaCT. Fig. 44B compares the amino acid sequences between human NaCT (amino acids 496-516) (SEQ ID NO: 30) and rat NaCT (amino acids 500-520) (SEQ ID NO: 31). The amino acids that are different between human and rat NaCTs are identified in bold. Fig. 44C shows substrate saturation kinetics of wild type human NaCT (●) and the Phe→Leu mutant of human NaCT (○). Fig. 44D demonstrates the influence of increasing concentrations of Li^+ on the uptake of citrate (20 μM) via wild type human NaCT (●) and the Phe→Leu mutant of human NaCT (○).--

Please replace the paragraph beginning at page 26, line 4, with the following amended paragraph.

--A pair-wise comparison analysis of transporter protein sequences can be carried out using the BESTFIT algorithm in the GCG package (version 10.2, Madison WI). Alternatively, polypeptides may be compared using the Blastp program of the BLAST 2 search algorithm, as described by ~~Tatiana~~ Tatsouva et al., (*FEMS Microbiol Lett*, 174, 247-250 (1999)), and available on the world wide web at ncbi.nlm.nih.gov/BLAST/. The default values for all BLAST 2 search parameters may be used, including matrix = BLOSUM62; open gap penalty = 11, extension gap penalty = 1, gap x_dropoff = 50, expect = 10, wordsize = 3, and filter on.--

Please replace the paragraph beginning at page 29, line 25, with the following amended paragraph.

--As used herein, "sequence identity" refers to the identity between two polynucleotide sequences. Sequence identity is generally determined by aligning the residues of the two polynucleotides (for example, aligning the nucleotide sequence of the candidate sequence and

the nucleotide sequence of SEQ ID NO:1, SEQ ID NO:3, SEQ ID NO:5, SEQ ID NO:7, SEQ ID NO:9, or SEQ ID NO:11) to optimize the number of identical nucleotides along the lengths of their sequences; gaps in either or both sequences are permitted in making the alignment in order to optimize the number of shared nucleotides, although the nucleotides in each sequence must nonetheless remain in their proper order. A candidate sequence is the sequence being compared to a known sequence, such as SEQ ID NO:1, SEQ ID NO:3, SEQ ID NO:5, SEQ ID NO:7, SEQ ID NO:9 or SEQ ID NO:11. For example, two polynucleotide sequences can be compared using the Blastn program of the BLAST 2 search algorithm, as described by ~~Tatiana~~ Tatsouva et al., *FEMS Microbiol Lett.*, 1999;174: 247-250, and available on the world wide web at ncbi.nlm.nih.gov/BLAST/. The default values for all BLAST 2 search parameters may be used, including reward for match = 1, penalty for mismatch = -2, open gap penalty = 5, extension gap penalty = 2, gap x_dropoff = 50, expect = 10, wordsize = 11, and filter on.--

Please replace the paragraph beginning at page 29, line 25, with the following amended paragraph.

--Vaccinia/T7 expression system. Functional expression of the ceNaCT cDNA in HRPE cells was done using the vaccinia virus expression system as described previously (Fei et al., *J Biol Chem* (2003);278: 6136-6144, Kekuda et al., *J Biol Chem* (1999);274: 3422-3429, Huang et al., *J Pharmacol Exp Ther* (2000);295: 392-403, Wang et al., *Am J Physiol Cell Physiol* (2000);278: C1019-1030, Inoue et al., *Biochem J*, (2002);367: 313-319, Inoue et al., (2002) *J Biol Chem* (2002);277: 39469-39476, Inoue et al., (2002) *Biochem Biophys Res Commun* (2002);299: 465- 471). HRPE cells grown in 24-well plates were infected with a recombinant vaccinia virus (VTF₇₋₃) at a multiplicity of 10 plaque-forming units/cell. The virus was allowed to adsorb for 30 minute at 37° C with gentle shaking of the plate. Cells were then transfected with the plasmid DNA (empty vector pSPORT or ceNaCT cDNA constructs) using the lipofection procedure (GIBCO-BRL, Gaithersburg, MD). The cells were incubated at 37° C for 12 hours and then used for determination of transport activity. Uptake of [¹⁴C]-citrate and [³H]-succinate was determined at 37° C as described previously (Inoue et al. (2002) *Biochem J* (2002);367: 313-319, Inoue et al., (2002) *J Biol Chem* (2002);277: 39469-39476, Inoue et al.,

(2002) *Biochem Biophys Res Commun* (2002);299: 465- 471). In most experiments, the uptake medium was 25 mM Hepes/Tris (pH 7.5) or 25 mM Mes/Tris (pH 6.5), containing 140, mM NaCl, 5.4 mM KCl, 1.8 mM CaCl₂, 0.8 mM MgSO₄, and 5 mM glucose. In experiments in which the cation and anion dependence of the transport process was investigated, NaCl was replaced isoosmotically by LiCl, KCl, sodium gluconate, or N-methyl-D-glucamine (NMDG) chloride. Uptake measurements were routinely made in parallel in control cells transfected with the plasmid alone and in cells transfected with the vector-cDNA construct. The uptake activity in cDNA-transfected cells was adjusted for the endogenous activity measured in control cells to calculate the cDNA-specific activity. Experiments were performed in triplicate and each experiment was repeated at least three times. Results are presented as means \pm S.E.--